The specification has been amended to reflect the two new Sequence ID Numbers 9 and 10, and to replace the previous Sequence Listing with the Substitute Sequence Listing submitted herewith in compliance with the Sequence Rules.

Figures 1B, 2B, 3A, 3B, 4, and 5 have been amended to insert SEQ ID NO designations as requested by the Examiner, solely to comply with the Sequence Rules.

Claims 18-39 were canceled as non-elected claims solely in response to the imposed restriction requirement. Claims 1, 2, 4, 5, 6, 10, and 11 were canceled solely to expedite prosecution, without acquiescing to the Examiner's position, and without prejudice to prosecution in a continuing application. New Claim 40 is directed to nucleic acid molecules of claim 3 that have particular nucleic acid sequences of SEQ ID NOs 1 and 3. Claim 3 has been amended to independent format and now recites nucleotide sequences encoding AL-2l, AL-2s, or AL-2 extracellular domain, essentially combining objected-to-claims 3, 4, and 6. Claim 12 has been amended to recite vectors containing the nucleic acids of claim 3 operably linked to a promoter Claim 13 has been amended to recite vectors of claim 12 having particular nucleotide sequences of SEQ ID NOs 1 and 3. Claim 14 has been amended to recite host cells having the vectors of claim 12, while claim 15 is directed to hosts of claim 14 having vectors with particular nucleotide sequences of SEQ ID NOs 1 and 3. Claim 17 has been amended to depend from claim 12. Claims 7 and 9 have been amended to depend from claim 3 and recite AL-2 extracellular domain fusions, of which claim 8 is a particular species presented in the specification.

No new matter has been introduced by these amendments.

Applicant appreciates the Examiner's use of the informal drawings and defers submission of formal drawings to correct objections noted by the Draftsperson until an indication of allowance is obtained. Please note the drawing amendments submitted herewith to comply with the Sequence rules.

Claims 1, 2, 5 ,7 , 8 , 9, 10, 11, 14, and 16 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification as to reasonably convey to one skilled in the relevant art that the inventor had possession of the

claimed invention at the time the application was filed. Without acquiescing to the Examiner's interpretation of the cited legal cases and patent policy in general on this issue, and solely to expedite prosecution, claims 1, 2, 5, 10, and 11 have been canceled. Claims 7, 8, 9, 14 and 16, which were included in this rejection apparently because of their ultimate dependence from claim 1, have been amended to depend ultimately from claim 3, which now recites nucleic acids comprising a nucleotide sequence encoding the amino acid sequence for mature AL-2l in SEQ ID NO: 2, a nucleotide sequence encoding the amino acid sequence for mature AL-2s in SEQ ID NO: 4, or a nucleotide sequence encoding the amino acid sequence of AL-2 extracellular domain in SEQ ID NO: 2--sequences which the Examiner viewed as adequately conveyed. Consequently, withdrawal of the rejection is respectfully requested.

Claims 1, 2, 5 ,7 , 8 , 9, 10, 11, 14, and 16 were rejected under 35 U.S.C. §112, first paragraph, as allegedly non-enabled by the specification for sequences having a recited degree of identity with SEQ ID NOs 2 or 4. Without acquiescing to the Examiner's position and solely to expedite prosecution, claims 1, 2, 5, 10, and 11 have been canceled. Claims 7, 8, 9, 14 and 16, which were included in this rejection apparently because of their ultimate dependence from claim 1, have been amended to depend ultimately from claim 3, which now recites nucleic acids comprising a nucleotide sequence encoding the amino acid sequence for mature AL-2l in SEQ ID NO: 2, a nucleotide sequence encoding the amino acid sequence for mature AL-2s in SEQ ID NO: 4, or a nucleotide sequence encoding the amino acid sequence of AL-2 extracellular domain in SEQ ID NO: 2--sequences which the Examiner viewed as adequately enabled. Applicant wishes to point out that a screen for AL-2 and its variants is reasonably conveyed. That a particular bioassay, which may be useful in such a screening process, is also specific to AL-2 is not a requirement for the screen to serve its useful purpose. Furthermore, protein sequences are in general quite fungible without a deleterious effect on protein activity or usefulness, as the cited references indicate (e.g., "proteins are suprisingly tolerant of amino acid substitutions" in Bowie *et al.* at page 1306). Typically, a protein active site (or receptor binding site) is limited to relatively small, definable region of the protein. As indicated in the cited references, this region is readily definable using known techniques, particularly when encoding DNA is available, as in the present case. Such a region is definable in part because it encompasses such a limited region of the protein. Conversely, the majority of positions along a protein backbone can typically be modified without serious consequence, a notion which the cited references support. Comparison of protein homologs across species generally supports this notion as well. Undue

experimentation is not required typically to identify regions that can be changed and to identify suitable changes within those regions. In any event, the issues of a screen and of protein fungibility aside, the pending claims are believed fully enabled, and withdrawal of the rejection is respectfully requested.

Claims 1, 2, 5 ,7 , 8 , 9, 10, 11, 14, and 16 were rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Claims 1, 2, 5 ,7, 8, 9, 10, 11, 14, and 16 were viewed as without determinable metes and bounds for not reciting "the particular means for determining sequence identity or homology" to SEQ ID NOs 2 or 4 "as compared to the entire sequence or as compared to a fraction or to a specific portion of the sequence." Applicant does respectfully submit that such language is well-accepted and understood in the art, whether a particular means is recited or not. The claims as originally drafted are not believed indefinite on this basis. Without acquiescing to the Examiner's position and solely to expedite prosecution, claims reciting this particular "hybridizing" language are no longer present amongst the pending claims. Consequently, pending claims 7, 8, 9, 14 and 16 have been amended in their dependency and no longer contain this particular recitation. Accordingly, the rejection should be withdrawn.

Claims 1 and 10 were rejected under 102(a) as anticipated by Hillier et al. (June 23, 1995), who discloses an EST sequence of 421 base pairs, which would hybridize to SEQ ID NOs 1 and 3 under stringent conditions and was alleged to "inherently encode a protein that is antigenically cross-reactive to mature human AL2-s or AL2-l." Claims 1 and 10 have been canceled solely to expedite prosecution, without acquiescing to the Examiner's position, and without prejudice to prosecution in a continuing application. It is not conceded that one of ordinary skill in the art had any motivation to use the EST sequence in the manner suggested by the Examiner, nor that one could be reasonably assured that the EST could have been used to generate even an immunologically active protein without undue experimentation without more regarding correct open reading frame, correspondence to the correct AL-2 sequence, and protein tissue source, for example. This issue aside, the rejection is rendered moot by cancellation of claims 1 and 10, and should be withdrawn.

Claims 1-17 were objected to as not complying with the Sequence Rules. Pending claims have been amended where particular sequences are mentioned to comply with the Sequence Rules. Withdrawal of the rejection to pending claims is requested.

Claim 13 was objected to as being of improper dependent form, depending from while identical in scope with Claim 12. Original claim 13 was narrower in scope than claim 12. Original claim 12 was directed to nucleic acid sequences encoding AL-2, while original claim 13 was directed to particular nucleic acid sequences shown in the figures; thus, claim 13 properly depended from claim 12. Claims 12 and 13, as amended, retain this relationship. Withdrawal of the objection is requested.

Claims 3, 4, 6, 12, 13, 15, and 17 were objected to as depending from a rejected base claim. Claims 4 and 6 have been combined into claim 3, with claim 3 amended to independent format. Claims 12, 13, 15 and 17 have been amended to remove dependencies to rejected claims and to depend ultimately depend from allowable claim 3. Withdrawal of the objection is requested.

In view of the above remarks, Applicant submits that this application is now ready for allowance. Early notice to this effect is solicited. If the Examiner believes a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at the number indicated below.

Respectfully submitted,
GENENTECH, INC.

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By: Timothy E. Torchia

Timothy E. Torchia, Ph.D.
Reg. No. 36,700

1 DNA Way
So. San Francisco, CA 94080-4990
Phone: (650) 225-8674
Fax: (650) 952-9881